Electrocatalytic oxidation of ketones

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The oxidation of ketones is a way for preparing carboxylic acids and their derivatives, bifunctional compounds such as α-hydroxyketones, diketones and other useful intermediates in organic synthesis. The formation of adipic acid from cyclohexanone is an important industrial process. In the case of aryl alkyl ketones the corresponding α-hydroxyketones and α-hydroxyketals are convenient compounds for synthesis of the pharmacologically active 2-arylalkanoic acids.[1]

The advance of electrooxidation procedures in recent years has provided organic chemists with a new synthetic device of great promise. But in the case of the electrooxidation of ketones only some reactions which could provide product-selectivity are known.

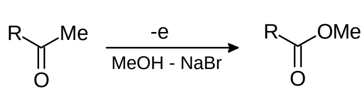
The first attempts of the electrochemical oxidation of ketones resulted in the formation of a mixture of acids, saturated and unsaturated hydrocarbons, carbon monoxide and dioxide.[2] Non selective remote oxidative functionalization of ketones was carried out in acetonitrile or trifluoroacetic acid as a result of the subsequent transformation of the initially produced cation radical $R^1R^2C{=}O^{+\cdot}$.[3] The anodic oxidation of cycloalkanones in aqueous alcohols usually gave mixtures of lactones of different types.[4]

In some oxidative transformations of ketones such as in the Favorskii rearrangement the preliminary α-halogenation of ketones is necessary. So for certain cases selective indirect electrooxidation of ketones with the electrochemically generated halides is also known.

The haloform reaction is often used for the conversion of methyl aryl ketones into carboxylic acids or esters. It has acquired importance primarily because of the fact that the introduction of a carboxyl group as substituent onto an aromatic ring is usually more difficult than the introduction of the acetyl group.

Methyl aryl ketones are generally converted into carboxylic acids by the action of halogen and sodium hydroxide.

We have realized the electrocatalytic variant of the haloform reaction. The electrolysis of aryl methyl ketones **1a-d** in an undivided cell in methanol in the presence of catalytic amount of sodium bromide leads to the corresponding methyl esters **2a-d** in 75-90% yields:



1a-d **2a-d**

a R=Ph; b R=4-MeC$_6$H$_4$; c R=4-MeOC$_6$H$_4$; d R=naphth-1-yl

The mechanism of the process:

at anode: $6Br^- - 6e \longrightarrow 3Br_2$

at cathode: $6MeOH + 6e \longrightarrow 6MeO^- + H_2$

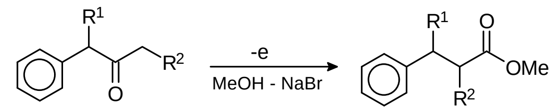
in solution: $RC(O)Me + 3Br_2 \longrightarrow RC(O)CBr_3 + 3H^+ + 3Br^-$

$RC(O)CBr_3 + MeO^- \longrightarrow RCOOMe + CBr_3^-$

$CBr_3^- + 2MeO^- + MeOH \longrightarrow HC(OMe)_3 + 3Br^-$

$$RC(O)Me + 4MeOH \xrightarrow[\text{MeOH - NaBr}]{\text{electrolysis}} RCOOMe + HC(OMe)_3 + H_2$$

Electrolysis of benzyl ketones **3a-c** under the same conditions led to esters **4a-c** in 50-60% yields:

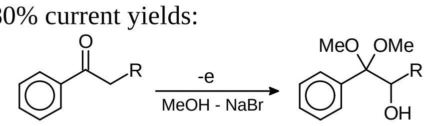


3a-c **4a-c**

a R^1=R^2=H; b R^1=H, R^2=Me; c R^1=Me, R^2=H

This process involves Favorskii rearrangement with participation of the electrochemically generated Br_2 and MeO^- ions. Using the NaI-NaOH mediatory system instead of NaBr increases yields of **4a-c** up to 80-90%.

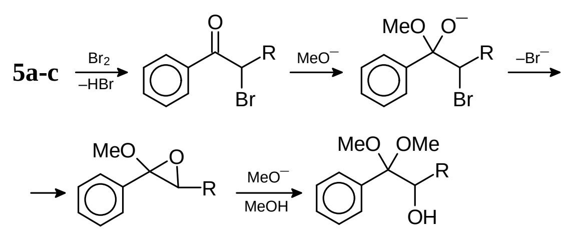
Phenyl alkyl ketones **5a-c** under the similar conditions with using mediatory system NaI-NaOH were converted into α–hydroxyketals **6a-c** in 75-85% substance yields and 70-80% current yields:



5a-c **6a-c**

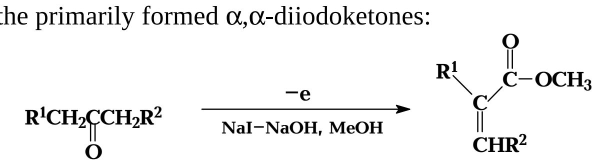
a R=Me; b R=Pr; c R=i-Pr

The mechanism of this process includes:



6a-c

Electrocatalytic oxidation of dialkyl ketones in methanol in an undivided cell in the presence of NaI-NaOH system leads to the corresponding unsaturated esters as a result of another type of the electrochemically induced Favorskii rearrangement with participation of the primarily formed α,α-diiodoketones:



The result of the electrocatalytic oxidation of cyclic ketones in methanol in an undivided cell in the presence of sodium iodide depends on the ring size. Cyclopentanone affords 2,2-dimethoxycyclopentanone. While cyclohexanone gives rise 2,2-dimethoxycyclo-hexanol, and cyclic ketones with higher ring size undergo new type of the electrochemically induced Favorskii rearrangement with the formation of methyl cycloalkenecarboxylates containing in the ring on the one carbon atom less than starting ketone. So the simple electrocatalytic system can distinguish the ring size of cyclic ketones.

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